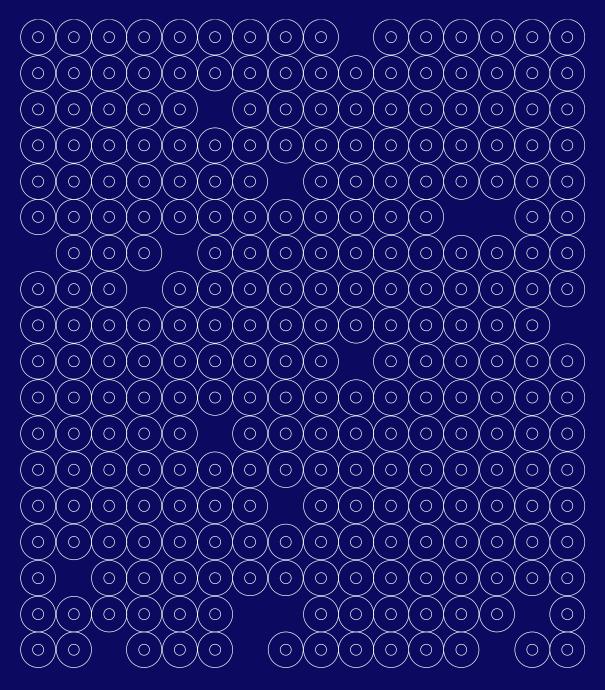
# JPIAMR Regional Workshop Asia

# Clinical Epidemiology, AMR policy, Therapeutics and

### Diagnostics

Suwon, Republic of Korea, 4-5 December 2019



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### Organised by Sungkyunkwan University School of Medicine

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## Introduction

#### **Background and workshop objectives**

In 2019, the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) focused on regional workshops around the world. The JPIAMR Regional Workshop Asia was organised by the JPIAMR member the Republic of Korea, with support from Japan. The objective of the workshop was to provide a forum for researchers and experts from Asian countries within the area of Antimicrobial Resistance (AMR) to come together and give insights into the AMR situation in different Asian countries, with a focus on clinical epidemiology, AMR policy, therapeutics and diagnostics.

The participants discussed differences, similarities, alignment and enhanced interactions in the region in a mixed forum of presentations and round-table discussions.

Major conclusions:

- The Antimicrobial Resistance focus across the Asia-Pacific region varies greatly from country to country, and from region to region within countries. This is a result of varying levels of antibiotic usage and different prevalence of bacteria resistant to antimicrobials in the community, healthcare, veterinary and environmental sectors across the continent.
- Most countries represented at the workshop have developed National Action Plans but there are challenges in the implementation of some of these plans.
- Access, rather than excess, is the reality in some Asian countries.
- The lack of regulation of antibiotic use in animal husbandry is a major issue in the Asian regions.
- Although research collaboration on AMR within and between Asian countries already exists, further support for collaboration in Asia should be encouraged, which needs increased dedicated funding and support to international collaborative efforts.



Figure 1. Participants at the JPIAMR regional workshop Asia

### **Organisers and Supporters**

#### Joint Programming Initiative on Antimicrobial Resistance (JPIAMR)

The Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) is a global collaborative platform engaging 27 nations to curb antibiotic resistance (AMR) with a One Health approach. The initiative coordinates national funding to support transnational research and activities within the six priority areas of the shared JPIAMR Strategic Research and Innovation Agenda – therapeutics, diagnostics, surveillance, transmission, environment and interventions. The JPIAMR is currently developing a platform to extend shared research capabilities on a global scale through the Virtual Research Institute (JPIAMR-VRI).

#### Sungkyunkwan University School of Medicine (SKKUSOM)

Sungkyunkwan University (SKKU) was founded in 1398 during the Joseon Dynasty but was officially reformed into a modern university in 1895. SKKU was promoted to a comprehensive university with the opening of its graduate school in 1953. In 1996, Samsung Group joined the University Foundation which was the beginning of an era of unbridled growth for SKKU. SKKU currently consists of 17 colleges and 47 departments with 4,700 faculties, 20,000 undergraduate students, and 7,000 graduate students. The SKKU School of Medicine was established in 1997 with Samsung Medical Centre (SMC) as an education hospital. The SKKU School of Medicine is ranked 37<sup>th</sup> in the world, and No.1 in Korea in the field of Clinical, Pre-Clinical & Health 2019 by Times Higher Education.

#### Institute of Antimicrobial Resistance Research and Therapeutics (IAMRT-SKKU)

The Institute of Antimicrobial Resistance Research and Therapeutics (IAMRT-SKKU) was launched at Sungkyunkwan University in 2018 with the aim to understand the principle of antibiotic resistance and to develop novel antimicrobial therapeutics. A key assignment for IAMRT-SKKU is conveying important research outputs and policy shifts to and from international communities working on AMR. Another key assignment of the centre is to coordinate all relevant research activities carried out by various ministries and agencies under one umbrella, subsequently leading to coordination not solely on a domestic level but on an international one.

#### National Research Foundation of Korea (NRF)

The National Research Foundation of Korea (NRF), supported from the ministry of science and Information and communications technology (ICT), was established in 2009. The NSF is a merger of Korea Science and Engineering Foundation (KOSEF), Korea Research Foundation (KRF), and Korea Foundation for International Cooperation of Science and Technology (KICOS) with the mission of "Contributing to the advancement of knowledge and improvement of quality of life through supporting creative research and fostering human resources". The total budget in 2019 was 5,236 million US dollars, which supports the basic research in science engineering (1,579 million USD), academic research in humanities and social sciences (205 million USD), national strategic R&D (1,669 million USD), academic promotion and cultivation of human resources (1,639 million USD), international affairs (73 million USD), and other research (71 million USD).

#### Japan Agency for Medical Research and Development (AMED)

The Japan Agency for Medical Research and Development (AMED) was established in 2015 for the advancement of medical discoveries that make life better for everyone. Working beneath the Prime Minister's Cabinet and national ministries, AMED promotes integrated research and development in the field of medicine, from basic research to clinical trials. Currently, 2,416 projects are supported by AMED. The total budget in 2019 was approximately 1,155 million USD.

#### Organising Committee

- Dr. Kyeong Kyu Kim, SKKUSOM, Republic of Korea
- Dr. Shoji Miyagawa, AMED, Japan
- Dr. Yumiko Miyashita, AMED, Japan
- Dr. Seon-Won Kim, NRF, Republic of Korea
- Dr. Akhilesh K. Chaurasia, SKKUSOM & IAMRT, Republic of Korea
- Dr. Laura Plant, JPIAMR, Sweden
- Dr. Jie-ming Qu, Medical School of Shanghai Jiaotong University, China

#### **Program Committee**

- Dr. Marc Lemonnier, JPIAMR Scientific Advisory Board, France
- Dr. You-Hee Cho, CHA University, Republic of Korea
- Dr. Kunihiko Nishino, Osaka University, Japan
- Dr. Xinshan Ye, Peking University, China
- Dr. Aixin Yan, University of Hong Kong, Hong Kong

#### Local Organising Committee

Ms. Sun Hee Kim, SKKUSOM, Republic of Korea

Ms. Nayab Batool, SKKUSOM, Republic of Korea

Dr. Truc Kim, SKKUSOM, Republic of Korea

Dr. Rekha Arya, SKKUSOM, Republic of Korea

Dr. Changsuk Oh, SKKUSOM, Republic of Korea

#### Chairs

Dr. Kyeong Kyu Kim, Director and Professor, Institute of Antimicrobial Resistance Research and Therapeutics (IAMRT), School of Medicine, Sungkyunkwan University, Suwon, Samsung Medical Centre, Seoul, Republic of Korea. Research Interests:

- 1. Structural and functional studies of non-canonical DNAs
- 2. Alternative strategies to combat against AMR

Dr. Jae-Seok Kim, Professor of Laboratory Medicine and Director of Clinical Microbiology in Kangdong Sacred Heart Hospital, Seoul, Republic of Korea. Research Interests:

- 1. Clinical diagnostic testing method for rapid, sensitive detection of pathogens
- 2. Molecular epidemiology and antimicrobial resistance of *Staphylococcus aureus*

Dr. Akhilesh K. Chaurasia, Research Professor, Institute of Antimicrobial Resistance Research and Therapeutics (IAMRT), School of Medicine, Sungkyunkwan University, Suwon, Republic of Korea. Research Interests:

- 1. Decoding the antimicrobial resistance using x-omics approach
- 2. Novel physical and mechanochemical approach to treat AMR infections

Dr. Sang Hee Lee, Professor, Division of Biosciences and Bioinformatics, Myongji University, Seoul, Republic of Korea. Research Interests:

- 1. Structural Proteomics of extended-spectrum  $\beta$ -lactamases, AmpCs, and carbapenemases
- 2. Structure-based drug design and target-oriented structural genomics

Dr. Laura Plant, Research Officer, Joint Programming Initiative on Antimicrobial Resistance (JPIAMR), Stockholm, Sweden. Interests:

- 1. Coordination of multi-sectorial One Health AMR research on a global scale
- 2. Funding research on the six priority areas of the JPIAMR Strategic Research and Innovation Agenda

Dr. Jae Hoon Yu, Director and Professor, Department of Chemistry & Education, Seoul National University, Seoul, Republic of Korea. Research Interests:

- 1. Cell penetrating peptides to increase passive permeability of larger cyclic peptides
- 2. Inhibition of protein-protein interaction

Dr. Kin-Ming (Clement) Tsui, Assistant Professor of Department of Pathology and Laboratory Medicine, Weill Cornell Medicine - Qatar; Pathology Sciences, Department of Pathology, Sidra Medicine, Doha, Qatar. Research Interests:

- 1. Population genetics and molecular epidemiology of pathogens to plants, animals and humans
- 2. Bioinformatic and molecular genetics approach to understand the evolution and antimicrobial resistance mechanisms of bacteria

Dr. Marc Lemonnier, Founding Chief Executive Officer (CEO) of Antabio, France; Scientific Advisor to JPIAMR. Research Interests:

- 1. Developing novel and proprietary anti-infectives targeting WHO's critical priority pathogens
- 2. Focus on small molecule inhibitors of carbapenemases to be combined with carbapenems for treating life-threatening infections

### **Keynote Sessions**

#### Keynote 1: Medicines policies and health systems

Socorro Escalante, World Health Organization

AMR is an ever-present threat to the achievement of universal health coverage (UHC), the Sustainable Development Goals (SDGs) and the security of populations. The complexity of the problem lies in its inherent nature and the characteristics and extent of its impact on health and development.

In 2014, the Regional Committee for the Western Pacific endorsed the Action Agenda for Antimicrobial Resistance in the Western Pacific Region, to guide countries in the development of national action plans, increase awareness on AMR other sectors and strengthen health systems and surveillance. Progress has been made, but many countries still face enormous challenges in tackling the drivers of AMR, particularly the overuse and misuse of antimicrobials, the spread and transmission of resistance and infections, and the contamination of the environment.

The Framework for Accelerating Action to Fight Antimicrobial Resistance in the Western Pacific Region, endorsed by the Member States of the Western Pacific, considers new ways of working to fight AMR. It will guide countries to implement sustained and futureoriented solutions through broad societal participation. Specifically, it will guide countries to: (i) Strengthen systems as foundation for sustainable actions (ii) Work beyond health (iii) Take actions today, guided by their vision of the future and (iv) Build solutions from the ground up, while ensuring country impact.

Dr. Socorro Escalante is currently the Coordinator for the programme on Essential Medicines and Health Technologies (EMT) and Antimicrobial Resistance (AMR) at the WHO Western Pacific Regional Office. She leads a team that supports countries to strengthen their national medicines policies and pharmaceutical systems to improve access to medicines. She spent a substantial part of her career working at the local government level, on legislations, hospital management, service delivery and primary health care. Dr. Escalante joined the WHO in 2006 working at the WHO Country Office in the Philippines, then in



WHO Country Office in Vietnam for eight years, prior to moving to the Regional Office in 2017. During her work at WHO, she received various recognitions such as Medal for the people's Health and Recognition for Contribution to the Social Security given by the Minister of Health and Vietnam Social Security. She received the WHO Reward of Excellence from the WHO Director General in 2016. Dr. Escalante is a Doctor of Medicine with degrees in Law and Masters of Business Administration in Health.

#### Keynote 2: JPIAMR: Global coordination of AMR research funding and activities

Laura Plant, Joint Programming on Antimicrobial Resistance (JPIAMR)

The Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) is comprised of 27 member nations that align to coordinate national research funding and coordination of multi-sectorial AMR research on a global scale. JPIAMR supports collaborative action for filling knowledge gaps on antimicrobial resistance with a One Health perspective. As well as accelerating the discovery of new antibacterial products, JPIAMR also supports research to better understand how resistance develops and spreads in the environment as well as the development of diagnostic tools, improved surveillance and intervention methods, and implementation of smarter strategies for using antibiotics in healthcare and agriculture. JPIAMR coordinates national public investments and funds transnational research and activities through the implementation of a shared JPIAMR Strategic Research and Innovation Agenda (SRIA). The six priority topics of the JPIAMR SRIA - therapeutics, diagnostics, surveillance, transmission, environment and interventions - provide the basis for JPIAMR joint actions. To date JPIAMR has supported 61 projects and 31 Networks with funding exceeding 80 million Euro. The JPIAMR is establishing the Virtual Research Institute in AMR, a Global Network connecting research performing organisations including institutes, centres, and infrastructures to each other across sectorial and geographic boundaries.

Dr. Laura Plant has a PhD. in Microbiology from the University of New South Wales in Australia. She completed postdoctoral studies at the Nestlé Research Centre in Switzerland, the University of Melbourne in Australia, and Karolinska Institutet in Sweden. Laura completed her Assistant Professorship at Karolinska Institutet in 2012 and in 2013 started to work with research funding as a Grants Officer at Karolinska Institutet. Laura jointed the Joint Programming Initiative on Antimicrobial Resistance as a Research Officer in 2017.



# Keynote 3: Novel antibacterials targeting WHO's critical priority pathogens: challenges and opportunities from discovery to commercialisation

Marc Lemonnier, Antabio, France

To defeat AMR under the One Health approach, the world needs a sustainable pipeline of novel antimicrobials, as well as strict stewardship rules to use them. The challenges faced by antimicrobial developers are diverse (scientific, regulatory, financial) and have recently escalated to a point where the whole antimicrobial development area is threatening to collapse. This presentation gave a review of the reasons for the strong headwinds currently faced by the industry, but also the opportunities offered by innovative companies (especially SMEs) that develop truly differentiated products addressing WHO's critical priority unmet needs.

Dr. Marc Lemonnier, founding CEO of Antabio, is a molecular and cellular microbiologist with over 25 years of experience in academia and biotech. Prior to founding Antabio, Marc held different research positions at various institutions globally such as CNRS and Inserm (France), CSIC (Spain) and Emory University (USA), authoring over 20 peer-reviewed articles in the field of bacterial pathogenesis and antibiotic resistance. Under Marc's leadership, Antabio has built a broad portfolio of novel and proprietary anti-infectives targeting WHO's critical priority pathogens, raised double-digit million funding and received numerous awards including a CARB-X award (2017) and



two Seeding Drug Discovery Awards from the Wellcome Trust (2013 and 2015). Marc is also a member of the Board of the BEAM Alliance (European Alliance of Biopharmaceutical companies combating Antimicrobial Resistance), and a member of the Scientific Advisory Board of JPIAMR (the Joint Programming Initiative on Antimicrobial Resistance).

#### Keynote 4: Diagnosis and combi-therapy against super-bacteria

Jun-Seob Kim<sup>1</sup>, Sun Young Kim<sup>1</sup>, Joon-hui Chung<sup>1</sup>, Chang-Jin Kim<sup>2</sup>, DongeunYong<sup>3</sup>, and Choong-Min Ryu<sup>1,\*</sup>

<sup>1</sup>Infectious Disease Research Center, KRIBB, Daejeon 34141, Republic of Korea.

<sup>2</sup> Industrial Bio-materials Research Center, KRIBB, Daejeon 34141, Republic of Korea.

<sup>3</sup> Department of Laboratory Medicine and Research Institute of Antimicrobial Resistance, Yonsei

University College of Medicine, Seoul 03722, Republic of Korea

Emergence and spread of human and animal pathogenic bacterial species, resistant to most of the available antimicrobial agents, is an area of great concern. AMR is now frequently associated with healthcare-associated infections. This presentation demonstrated a novel combination therapy and diagnosis of AMR bacteria. For combination therapy, the group employed the large-scale screening of Streptomyces secondary metabolites and chemical library to search for adjuvants of a last resort to the antibiotic polymyxin B. The recent emergence of polymyxin-resistant bacteria, however, urgently demands clinical optimisation of polymyxin use to minimise further evolution of resistance. This group identified a reliable polymyxin synergist, which was confirmed to be netropsin, using high-pressure liquid chromatography, nuclear magnetic resonance, and mass spectrometry, followed by in vitro assays using various Gram-negative pathogenic bacteria. To evaluate the effectiveness of combining polymixin B and netropsin in vivo, the group performed survival analysis on the greater wax moth Galleria mellonella after infection with colistin-resistant clinical Acinetobacter baumannii isolates as well as Escherichia coli, Shigella flexineri, Salmonella typhimurium, and Pseudomonas aeruginosa. Additionally, to diagnose infection with AMR bacteria, metagenomic and genome-wide target gene analysis was utilised to obtain species specific and AMR genes for molecular detection. Collectively, the acute diagnosis and effective usage of antibiotics can be critical step to control AMR bacteria.

Dr. Choong-Min Ryu is a principal research scientist at the Korea Research Institute of Bioscience and Biotechnology, Republic of Korea. After completing his PhD at Auburn University, USA where he discovered that bacterial volatiles elicit plant growth promotion and plant immune responses, he moved to The Samuel Robert Noble Foundation for a postdoctoral position. His research topics include: 1) bacterial volatile-mediated inter- and intra-specific communication, 2) developing antibiotics and their adjuvants from synthetic chemical and biogenic compounds. Prof. Ryu is currently serving as a specialty chief editor of the Plant Microbe Interaction session of Frontiers in



Microbiology and Frontiers in Plant Science, and is an editorial member of PLOS One. Prof. Ryu has published more than 150 peer-reviewed high impacts research papers with several discoveries in the fields in the plant/microbe interactions and antimicrobial resistance.

### Sessions

#### Session 1-1: Clinical and molecular characteristics of rapid-spreading carbapenemresistant *Enterobacteriaceae* in China

Jie-Ming Qu, Rui Jin Hospital, Shanghai Jiaotong University School of Medicine, China

The prevalence and carbapenem resistance rates of *Klebsiella pneumoniae*, which is one of the top five major species isolated from clinical specimens, are persistently increasing in China, urging us to better understand this challenging strain and investigate potential targets for novel drug development. Genetic diversity, rapid evolution and multiple resistant mechanisms of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) further complicate the problem. This presentation described the prevalence and molecular epidemiology of CRKP according to the results from national antimicrobial surveillance network and published data, implicating the current status and trends in antimicrobial resistance. The presentation addressed risk factors, current treatments, prognosis and medical costs of infections caused by carbapenem-susceptible *Klebsiella pneumoniae* (CSKP) and CRKP. Hospital infection measures and antimicrobial stewardship procedures in China to limit the emergence and dissemination of CRKP were presented.



Dr. Jie-Ming Qu is a doctoral and postdoctoral graduate tutor and has been selected for the Shanghai leading talent program. He currently serves as President of Ruijin Hospital, Medical School of Shanghai Jiaotong University; Chairman designate of respiratory branch of Chinese Medical Association and Head of the pulmonary infection group; Vice chairman of the respiratory branch of the Chinese Medical Association; chairman of the Respiratory Society of the Shanghai Medical Association and Director of Institute of Respiratory Diseases, Medical school of Shanghai Jiao-tong University School. His research is supported by National Natural

Science Foundation of China (eight projects) and National Key Basic Research program (two subprojects), and he has been awarded for National Science and Technology Progress Award (2<sup>nd</sup> prize) and municipal Science and Technology Progress Award (2<sup>nd</sup> prize). He has more than 300 publications (total IF 320). He also has a considerable experience in publishing eight monographs as either editor-in-chief or associate editor. Research Interests:

- 1. The pathogenic epidemiology of the lower respiratory tract infection and its clinical diagnosis and treatment
- 2. The treatment effects and mechanism of mesenchymal stem cells in severe pulmonary infection
- 3. The relationship between microbe balance and respiratory disease in the lower respiratory tract

#### Session 1-2: Antimicrobial resistance (AMR) in Japan

Yohei Doi, Fujita Health University School of Medicine, Japan

Japan built a robust antibiotic industry after World War II and many antibiotics currently in use were discovered or developed there. Despite this legacy, the overall antimicrobial consumption is relatively low and decreasing, thanks to a renewed focus on antimicrobial stewardship. However, the majority of antibiotic use is concentrated on broad-spectrum classes including marcolides, cephalosporins and fluoroquinolones. Common AMR pathogens in Japan include methicillin-resistant Staphylococcus pneumoniae, aureus (MRSA), drug-resistant Streptococcus ampicillinresistant Haemophilus influenzae, extensively drug-resistant Neisseria gonorrhoeae, and ESBL-producing Escherichia coli. On the other hand, vancomycin-resistant enterococci (VRE), carbapenem-resistant Enterobacteriaceae (CRE), multidrug-resistant (MDR) Pseudomonas aeruginosa and multidrug-resistant Acinetobacter baumannii remain rare. In Japan, it appears that community-associated pathogens are currently more problematic than healthcare-associated pathogens in terms of AMR.



Dr. Yohei Doi is Professor of Microbiology and Infectious Diseases at Fujita Health University and Associate Professor of Medicine and Director of the Center for Innovative Antimicrobial Therapy at the University of Pittsburgh. He graduated from Nagoya University School of Medicine in Nagoya, Japan. After training in internal medicine and basic research on characterisation of novel antimicrobial resistance mechanisms in Gram-negative pathogens, he moved to the USA to further pursue clinical training, completing residency in categorical medicine at St. Luke's Roosevelt Hospital Center, followed by an infectious diseases fellowship at the University of Pittsburgh where he also received training in clinical and translational research. His

research focuses on mechanisms of antimicrobial resistance in highly drug-resistant Gramnegative bacterial pathogens and devising ways to overcome the resistance mechanisms. He has authored over 200 articles in peer-reviewed journals and mentored over 30 students and trainees in his laboratory. He currently chairs the Gram-negative committee of the Antibacterial Resistance Leadership Group.

#### Session 1-3: Current status of AMR in humans in South Korea: a report from Kor-GLASS

Seok Hoon Jeong, Department of Laboratory Medicine and Research Institute of Bacterial Resistance, Yonsei University College of Medicine, Republic of Korea

At the end of 2015, a global action plan on AMR was proposed by the World Health Organization (WHO), and the Global AMR Surveillance System (GLASS) was subsequently initiated to gather the necessary evidence to guide further policy and decision making. The GLASS protocol was generated to standardise the surveillance methods to enable a comparative overview of global AMR. With the advent of the new system in early 2016, the Centres for Disease Control and Prevention of South Korea (KCDC) established a customised AMR surveillance system for South Korea, Kor-GLASS, replacing the existing lab-monitoring-based surveillance system, the Korean AMR Monitoring System (KARMS). Following the principles of GLASS, including representativeness, specialisation, harmonisation, and localisation, all non-duplicate clinical isolates of major pathogens were collected from sentinel hospitals across the Korean peninsula along with the clinical data of the patients. A pilot phase of Kor-GLASS was operated from May to December 2016 with six sentinel hospitals, and the established system received good reviews internationally as a desirable example of AMR surveillance. The success of the pilot phase of Kor-GLASS encouraged the KCDC to expand the system by increasing the number of sentinel hospitals from six in the pilot phase to eight in phase I (2017-2019) and 11 in phase II (2020-2022). During the pilot phase, Kor-GLASS was reinforced by establishing two supplemental structures: (i) a quality control centre for ensuring the accuracy of the results from the analysis centre by performing parallel tests and (ii) a web-based data-managing constitution for clinical data from sentinel hospitals, laboratory data from the analysis centre, and parallel test results from the quality control centre. The phase I of Kor-GLASS started in January 2017 with eight sentinel hospitals and is now in its third year. The blood isolates from the one-year assessment in 2017 were presented, with their characteristics and the clinical information of the patients with bacteremia caused by nine major pathogens.

Dr. Seok Hoon Jeong (M.D. PhD.) is a Professor at the Department of Laboratory Medicine and the Research Institute of Bacterial Resistance, Yonsei University College of Medicine, Seoul, Republic of Korea. He is also Director at the Department of Laboratory Medicine at Gangnam Severance Hospital. Dr Jeong is an Editor of the International Journal of Antimicrobial Agents and the Director of the Planning Committee for the Korean Society of Clinical Microbiology. He has a PhD in Laboratory Medicine from Busan National University Graduate School, Busan and has a background from Yonsei University College of Medicine, Seoul, as well as a Master of Medicine, Clinical Pathology, Yonsei University Graduate School.



# Session 1-4: National action plans to combat antimicrobial resistance (AMR) in Vietnam and the high prevalence of AMR bacteria in community

Hoa Thi Ngo, Zoonoses Group Oxford University Clinical Research Unit, Vietnam

The Ministries of Health and Agriculture and Rural Development in Vietnam ratified and promulgated the National action plans to combat AMR in humans, on antimicrobial usage (AMU) and management, as well as AMR prevention in animal husbandry and aquaculture, in 2013 and 2017. Both of the plans will be effective until 2020 but have different roadmaps due to the existence of different purposes of AMU for human and animals and in aquaculture, as well as differences in the support systems during implementation. Our studies focus on providing local research-based AMR data to local animal producers and policy makers, as well as understanding their perceptions and practices regarding AMU, as well as a potential mitigation plan on reducing the impact of the withdrawal of antimicrobials for growth promotion in animal husbandry. The high levels of AMR bacteria that were detected could be explained by AMU in the community, which were believed by farmers to be practised with considered manner.

Dr. Ngo, Thi Hoa obtained her PhD. in molecular microbiology from Royal Holloway, University of London, UK (1998-2001). Dr. Hoa focuses on research related to improvement of community health on prevention of infectious disease transmission and the promotion of responsible use of antimicrobials by employing multidisciplinary approaches. Dr. Hoa is the Head of the Zoonoses Group Oxford University Clinical Research Unit in Vietnam. She studies zoonosis infection with a focus on: 1) Improving diagnostics, investigating virulence, pathogenesis, epidemiology and immunology



of Streptococcus suis infection, 2) Investigating AMU and AMR in bacteria with their potential zoonotic transmission via agriculture/farming/food chain production, 3) Identifying potential and feasible interventions to reduce zoonotic transmission and AMU, and 4) Improving knowledge and change behaviors via public engagement activities and social science. Dr. Hoa has authored more than 60 research papers describing the AMR of various high priority pathogens. She is also affiliated with University of Science, National University in HCMC, and Pham Ngoc Thach Medical University, Vietnam. With local research experience, she leads OUCRU team working with the team from Myanmar Partner from Livestock Breeding Veterinary Department (LBVD) in the Myanmar Pig Partnership (MPP) project. She is one of the co-PIs of the JPIAMR project aiming to understand the impact of host restriction of E. coli on transmission dynamics and spread of antimicrobial resistance (HECTOR).

#### Session 2-1: Antimicrobial resistance (AMR) policy update in Asia

Isabel Frost, The Centre for Disease Dynamics, Economics & Policy (CDDEP), India

Antimicrobial resistance has been recognised as a global threat to health (1) with further reaching implications for sustainable development (2). This issue is becoming increasingly important worldwide, but it particularly affects South Asia, where access to clean water, sanitation, and appropriate levels of hygiene is often limited, facilitating the spread of infection. This is compounded by widespread over-the-counter availability of antibiotics, contributing to the overuse of this scarce resource and selection for resistance (3). Over 58,000 deaths a year in India are due to two common resistant organisms: extended-spectrum beta-lactamase producers and methicillin-resistant *Staphylococcus aureus* (MRSA) (4). Drug resistance in typhoid, hospital acquired infections harder to treat effectively (5). In response this, all countries in the region now have National Action Plans however the upcoming challenge will be to operationalise these.

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4. Laxminarayan R, et al. (2013) Antibiotic resistance-the need for global solutions. Lancet Infect Dis 13(12):1057–98.

5. Gandra S, Joshi J, Trett A, Sankhil Lamkang A, Laxminarayan R (2017) Scoping Report on Antimicrobial Resistance in India Available at: <u>https://cddep.org/wp-content/uploads/2017/11/AMR-INDIA-SCOPING-REPORT.pdf</u>

ACKNOWLEDGEMENT: Jyoti Joshi (Head CDDEP Asia), Ramanan Laxminarayan (Director, CDDEP)

Dr. Isabel Frost is currently a research fellow at the Center for Disease Dynamics, Economics & Policy in the New Delhi office, where she has been based for the past two years. Dr. Frost received her PhD from the University of Oxford doing research to better understand the evolution of antimicrobial resistance (AMR) and how we can best use antimicrobial drugs while preventing the emergence of resistance. Dr. Frost is currently working on a variety of projects, with the aim of applying these ideas in global health, particularly in the developing world. These projects include an interest in how vaccines can combat AMR and in how consumer goods distribution networks can be co-



opted to spread vaccine messaging to rural areas. Dr. Frost is currently also involved a study that looks for AMR genes in hospital waste. Her research has investigated the barriers to access to antibiotics in India and further afield. Her research background in AMR is supplemented by science policy experience with both the World Health Organisation and British Parliament. Dr. Frost is also an honorary research fellow at Imperial College London, UK, Department of Medicine and a postdoctoral research fellow at Amity University, India, Department of Public Health. Work Interests: 1. Global Health, 2. Antimicrobial resistance, and 3. Vaccines

#### Session 2-2: Containing AMR, China's action

Yuxing Ni, Dept. of Clinical Microbiology and Infection Control, Rui Jin Hospital, China

Antimicrobial resistance is presently one of the biggest public health challenges. It has the potential to affect people at any stage of life, making it one of the world's most urgent public health problems. In China, much attention is focused on AMR. From 2013-2018, the antibiotic use intensity (DDD) in general hospitals decreased. Bacterial resistance of five major clinical isolates (except the Carbapenem-resistant *Klebsiella pneumoniae*) showed a decreasing resistance trend. The government has taken ambitious steps to fight the AMR threat. For example, it implemented national laws and regulations and improved AMS specifications, established MDT mechanism and strengthened the management of use of antibiotics in children.

Dr. Yuxing Ni is Director of clinical microbiology department and Director of nosocomial infection control department of Ruijin Hospital Affiliated to Shanghai Jiaotong University Medical College. He has a Bachelor of medicine in 1977 from Bengbu Medical College, P.R.China; 1983, Master of medicine from Bengbu Medical College, P.R.China; 1989, PhD in medical science from Institute of Microbial Diseases, Osaka University, Japan; 1992 and Scholar researcher in Department of Microbiology, Chinese University of Hong Kong. Research Interests: Clinical microbiology detection, Bacteria resistance mechanism and Antimicrobial stewardship.

#### Session 2-3: National action plan on AMR and R&D funding in Japan

Shoji Miyagawa, The Japan Agency for Medical Research and Development (AMED), Japan

The Government of Japan launched the National Action Plan on Antimicrobial Resistance (AMR) in April 2016 in which six goals and their specific strategies were identified. The goals are; 1) Improve public awareness and understanding, and promote education and training of professionals, 2) Continuously monitor antimicrobial resistance and use of antimicrobials, and appropriately understand the signs of change and spread of antimicrobial resistance, 3) Prevent the spread of antimicrobial-resistant organisms by implementing appropriate infection prevention and control, 4) Promote appropriate use of antimicrobials in the fields of healthcare, livestock production and aquaculture, 5) Promote research on antimicrobial resistance and foster research and development to secure the means to prevent, diagnose and treat antimicrobial resistant infections, and 6) Enhance global multidisciplinary countermeasures against antimicrobial resistance. Regarding research and development activities on AMR, AMED organises a public - private partnership by participation from academia and industry to promote R&D activities on AMR in particular on development of new antibiotics.



Dr. Shoji Miyagawa is Senior Manager, Department of Research Promotion, Division of Infectious Disease Research, the Japan Agency for Medical Research and Development (AMED), Japan since August 2017. He is also appointed Counsellor, Health Service Bureau, Ministry of Health, Labour and Welfare (MHLW), the Government of Japan. Before his secondment to AMED, he has been Director, Infectious Disease Information Surveillance Office, Tuberculosis and Infectious Disease Control Division, Health Service Bureau, MHLW/GOJ since April 2015, Director, Division of

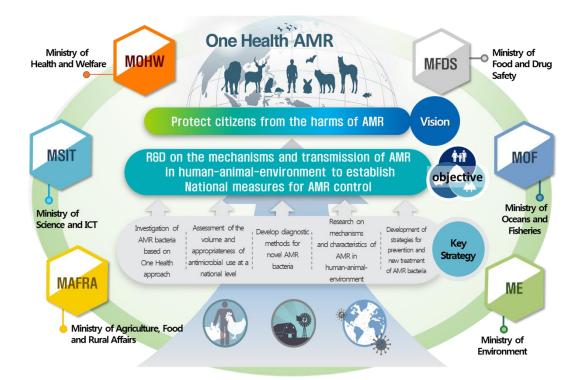
International Cooperation, the National Institute of Infectious Diseases (NIID) since July 2011, and Counsellor, Permanent Mission of Japan to the United Nations, New York, USA since May 2008. He has been serving various positions mainly on public health in the Ministry of Health, Labour and Welfare since he joined the Ministry in 1987. He graduated from the Veterinary School of the Osaka Prefecture University in 1987.

# Session 2-4: One Health Approach to combat AMR in Korea; Multi-sectoral AMR research strategies & activities

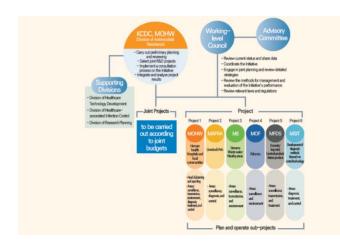
Kwang-Jun Lee, Centre for Disease Control and Prevention, Korea

Over the past decades, several efforts have been already made at the national and international level to address antimicrobial resistance (AMR) in the human sector, but it turns out to be a failure. Nowadays, antimicrobial resistance (AMR) has become a globally hot issue in human health.

The Korean government has been taking actions to optimise the usage of antimicrobials in the hospitals of human sector, and prohibit in-feed use of antimicrobials for growth promotion in the livestock sector. Despite long-term efforts, the total consumption of antimicrobials is still increasing and in Korea is the highest compared with other OECD countries. This excessiveness is attributed to acceleration of multidrug-resistant bacteria in human and non-human sectors in Korea. There is a growing awareness that widespread excessive use of antimicrobials across livestock, agriculture, and aquaculture can cause the emergence of AMR bacteria in humans through diverse paths. Therefore, we focused on the necessities of the coordinated One Health approach on AMR to tackle AMR in Korea.



In 2016, the Korean government established a National Action Plan on AMR (NAP) over five-year period (2016-2020) with the AMR consultative committee of five ministries. Since then, the Korean NIH built on the multi-sectorial One Health AMR R&D Initiative to improve the integrated understanding of AMR across human and non-human such as livestock, companion animal, food, and the environment to reduce spread and impact of AMR bacteria, in collaboration with Ministry of Health and Welfare, Ministry of Agriculture, Food, and Rural Affairs, Ministry of Oceans and Fisheries, Ministry of Food and Drug Safety, and Ministry of Environment. Korea has worked with multiple research groups to support better understanding of resistant bacteria across sectors and to build on a One Health approach to recognise the integrated complex interactions that contribute to AMR.



The One Health AMR R&D Initiative defines three priority fields; 1) Surveillance of AMR in one-health settings, 2) Mechanism and transmission of AMR across sectors. 3) Infrastructure for One Health AMR R&D. There are ongoing three surveillance systems of AMR based on a One Health approach: the livestockrelated, the companion

animal-related, and the hospital-related. This can provide data of AMR within a One Health perspective and support research of transmission of AMR bacteria and resistance genes between humans, animals, and the environment. However, there is so much more still to do. An integrated understanding of the spread of AMR across sectors remains poorly understood. This surveillance-related research offers an opportunity to understand the complexity of how resistance is spread, and help develop our own evidence-based intervention strategies for reducing of AMR with the One Health perspective. In addition, we focus on antibiotics usage and its appropriate evaluation, development of diagnostic methods and new therapeutics of AMR bacteria. Strong cooperation efforts of multidisciplinary research groups are the cornerstone for assessing AMR burden across the sectors. Additionally, it will provide the evidence base to support decision-making action of AMR intervention for achieving the health in human and non-human sectors at national level.

Dr. Kwang-Jun Lee is Deputy Scientific Director at Division of Antimicrobial Resistance, Korea National Institute of Health (KNIH). He completed his PhD at the Department of Microbiology, Chungbuk National University in Korea. He worked at Division of Bacteria, National Institute of Infectious Diseases (NIID) as a Post Doc in Japan for two years since 2000-2001 and he served as director of the Pathogen Resource task force for three years. His recent research projects have been focused on "Antimicrobial Resistance". He managed the Kor-GLASS project compatible with WHO GLASS, and he has been managing and carrying out "Multi-sectoral Joint Project One Health approach against Antimicrobial Resistance" since 2017, coordinated with related ministries.



# Session 3-1: Native CRISPR-Cas mediated genome editing facilitates the treatment of clinical multidrug resistant *Pseudomonas aeruginosa* based on collateral sensitivity

Aixin Yan, The University of Hong Kong, Hong Kong

Despite being fundamentally important and having direct therapeutic implications, the functional genomics of the clinical isolates of multidrug-resistant (MDR) pathogens is often impeded by the lack of genome-editing tools. To overcome this impediment, we established a highly efficient *in situ* genome editing technique applicable in clinical and environmental isolates of the prototypic MDR pathogen *P. aeruginosa* by harnessing the endogenous type I-F CRISPR-Cas systems. Using this approach, we generated various reverse mutations in an epidemic MDR genotype, PA154197, and identified underlying resistance mechanisms that involve the extensive synergy among three different resistance determinants. Screening a series of "ancestor" mutant lines uncovered the remarkable sensitivity of the MDR line PA154197 to a class of small, cationic peptidomimetics, which sensitise PA154197 cells to antibiotics by perturbing outermembrane permeability. These studies provide a framework for molecular genetics and anti-resistance drug discovery for clinically isolated MDR pathogens.

Dr. Aixin Yan is currently an Associate Professor at School of Biological Sciences, laboratory of Molecular Microbiology and Biochemistry in The University of Hong Kong, Hong Kong SAR. Dr. Yan received several prestigious Fellowships and Awards in the field of Molecular Microbiology and Biochemistry. She is the member of various Molecular Biology, Biochemistry and Microbiological Societies including the Program committee of the JPIAMR regional workshop in Asia 2019. Her broad area of research includes 'Antimicrobial resistance and its interplay with the virulence and physiology in Gramnegative bacteria', 'Metal homeostasis and heavy metal resistance', and 'CRISPR-Cas systems in Pseudomonas aeruginosa and their



exploitations in anti-resistance drug development'. She established genome-editing techniques in the non-model, clinical P. aeruginosa isolates by repurposing the endogenous type I-F CRISPR-Cas system in these strains and developed collateral agents to sensitise MDR strains to antibiotics. Her work provides framework to genome editing and anti-resistance drug development in clinical MDR pathogens. Dr. Yan has published more than sixty peer-reviewed publication in the journal of repute.

# Session 3-2: Antibiotics Pipeline for Infectious Diseases and Development Strategy of LegoChem Biosciences, Inc

Young Lag Cho, LegoChem Biosciences, Korea

The severity of infectious diseases has emerged as a global problem and it has been reported that 10 million people will die from antibiotic resistance by 2050. However, despite the seriousness, the development of antibiotics is extremely slow and resistant Gram-negative bacteria are almost impossible to treat with existing drugs. The increase of multi-drug resistant (MDR) strains of these pathogens has been associated with prolonged hospital stays, higher health care costs, and increased mortality. However, we have not enough pipeline drugs yet. LegoChem has been engaged in antibiotic development since its foundation in 2006 and has introduced new oxazolidinone and cepha antibiotics into the clinical trials. The new oxazolidinone, Delpazolid (LCB01-0371) is effective against tuberculosis as well as Gram-positives (MRSA, VRE). The other pipeline GT-1(LCB10-0200) is new Cephalosporin antimicrobial, which is active against problematic gram negatives including MDR-PA and MDR-AB.

Dr Young Lag Cho is the Chief Development Officer of LegoChem Biosciences, Inc., Daejeon, Korea (2006 – Present), where he is the project leader of antibiotics and anticoagulants program and worked with the development of antibiotics (preclinic ~phase 2). He worked previously at The LG Life Science Research Institute, Daejeon, Korea (2001 –2006), and has been a senior researcher in the development of beta secretease inhibitor for Alzheimer disease. Dr Young Lag Cho received his PhD from Yonsei University in Korea and completed postdoctoral positions at The Salk Institute and The Scripps Research Institute.



#### Session 3-3: Multidrug efflux pumps in Gram-negative bacteria

Kunihiko Nishino, Osaka University, Japan

Multidrug efflux is an obstacle to the successful treatment of infectious diseases, and it is mediated by multidrug efflux pumps that recognise and export a broad spectrum of chemically dissimilar toxic compounds. Many bacterial genome sequences have been determined, allowing us to identify drug efflux genes encoded in the bacterial genome. By the postgenomic approach, we have identified drug efflux genes and their regulatory networks in Gram-negative bacteria. Multidrug efflux pumps are often regulated by environmental signals and they are required for bacterial virulence in addition to multidrug resistance. It is now understood that these efflux pumps also have physiological roles. We investigated the physiological roles of drug efflux pumps in virulence. Because multidrug efflux pumps have roles in bacterial drug resistance and virulence, we propose that drug efflux pumps have greater clinical relevance than previously considered.

Dr. Kunihiko Nishino is Professor at Institute of Scientific and Industrial Research, and Graduate School of Pharmaceutical Sciences, Osaka University, Japan. He has a PhD in Pharmaceutic Science from Osaka University in Japan and postdoctoral training from the Japan Society for the Promotion of Science from the Washington University School of Medicine in St. Louis.



#### Session 3-4: From antibiotic to anti-virulence for AMR infection

Cai-Guang Yang, Shanghai Institute of Materia Medica, China

In order to reverse the rapid emergence of AMR, antimicrobial drug discovery must find new approaches alternative to the existing antibiotics, in particular those with novel modes of action. The natural product ADEPs have been identified as a new class of antibiotics that activate bacterial ClpP in dysfunctional state. In the combinative usage with classic antibiotics, ADEP eradicates a deep-seated persister. These findings indicate a general principle for killing dormant cells—activation and corruption of a target, rather than inhibition. We have engineered a ClpP mutant system in a gain-of-function state, which mimics the treatment of wild type ClpP with the activator ADEP. In addition, our current research focuses on the development of small-molecule modulators to target ClpP for antibacterial infection. We are also interested in chemical inhibition of bacterial virulence for treating AMR infection. The sortase A has been suggested as a potential target for anti-virulence drug discovery. We have performed a computational screening and synthetic optimisation, which afforded compound 6e as a new scaffold inhibitor that displays broad-spectrum activity to inhibit sortase activity in the Gram-positive bacteria. Different assays were carried out in order to understand the inhibitor mode of action. The inhibitors 6e minimally affected the in vitro growth of S. aureus even in high concentration, however, it protected mice against lethal S. aureus bacteremia, for example MRSA USA300. Thus, sortase inhibitors may be useful as anti-infective therapy to prevent S. aureus infection without the side effects of antibiotics.

Dr. Cai-Guang Yang received a Bachelor of Science degree in Chemical Engineering from Huazhong University of Science and Technology and earned a PhD in Organic Chemistry from Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences. He received his postdoctoral training in Structure Biology in the Chemistry Department at the University of Chicago. In 2008, he was recruited to Shanghai Institute of Materia Medica, Chinese Academy of Sciences, where he was appointed as a full professor. Current research in his lab centers on the discovery of small-molecule modulators targeting the untargeted proteins in order to probe biology and eventually develop new medicine.

#### Session 3-5: Chemical modifications of aminoglycoside antibiotics and beyond

#### Xin-Shan Ye, Peking University, China

Aminoglycosides are a group of well-known antibiotics, which function through binding to specific sites in prokaryotic ribosomal RNA (rRNA) and affecting the fidelity of protein synthesis. Unfortunately, their clinical use has been curtailed by toxicity and a rapidly increasing number of resistant strains. Therefore, it is highly desirable to design new modified aminoglycosides that will overcome the undesirable properties of natural occurring aminoglycosides. Herein we described our efforts to find new aminoglycoside derivatives based on modifications or reconstructions of aminoglycoside antibiotics. The biological evaluations showed that some synthetic compounds might hold the potential as antibacterial agents.<sup>1-4</sup> On the other hand, utilising dimerisation strategy, we rationally designed and efficiently synthesised a new series of small molecule dimeric lysine alkylamides as mimics of antimicrobial peptides (AMPs). Evaluation of these mimics against a panel of Gram-positive and Gram-negative bacteria including multidrug resistant (MDR) strains was performed, and the broad-spectrum and potent compound was identified. The results suggested that dimeric Lysine N-Alkylamides has immense potential as a new type of novel small molecular agent to combat antibiotic resistance.<sup>5</sup>

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Dr. Xin-Shan Ye received his B.S. and M.S. degrees from Wuhan University in 1985 and in 1988, respectively. He was appointed as a lecturer at Huazhong Agricultural University from 1988 to 1993. Then he spent three years in Hong Kong for his doctoral study and obtained his PhD degree from The Chinese University of Hong Kong in 1996 under the direction of Prof. Henry Wong. After three and a half years of post-doctoral research with Prof. Chi-Huey Wong at The Scripps Research Institute, he went back to China in 2000 and was appointed as Changjiang Professor of Medicinal Chemistry at Peking University. The research of the Ye group deals with chemical glycobiology and carbohydrate-based drug discovery. The research interests include the development of new methodologies or strategies for the assembly of oligosaccharides, the synthesis and evaluation of biologically important oligosaccharides such as tumor-associated antigens, modifications of aminoglycoside antibiotics, as well as the design, synthesis and evaluation of carbohydrate-processing enzyme inhibitors. Dr. Ye has published more than 140 scientific papers in international peer-reviewed journals. Some results of his research work was highlighted five times by scientific journals such as Science and C&EN. He has one Japanese patent, two US patents and ten Chinese patents.

# Session 4-1: Holotomography and artificial intelligence: label-free 3D imaging and analysis of individual live cells

YongKeun Park, Department of Physics, Korean Advanced Institute of Science and Technology, Daejeon 34141, Republic of Korea and Tomocube Inc., Daejeon 34051, Republic of Korea

We present a rapid and label-free method for single-cell analysis, utilising quantitative phase imaging (QPI) and machine learning. Holotomography (HT), one of the 3D QPI techniques, uses laser interferometry to measure 3-D refractive index (RI) distribution. HT serves as a powerful tool for imaging small transparent objects, such as biological cells and tissues. HT is an optical analogous to X-ray computed tomography (CT); HT measured multiple 2-D holograms of a sample with various illumination angles, from which a 3-D RI distribution of the sample is reconstructed by inversely solving the wave equation. Unlike conventional fluorescence-based imaging techniques, HT provides label-free 3-D imaging capability. Without any fixation or labeling, 3-D images of live cells can be obtained with high spatial resolution (down to 110 nm) and high temporal resolution (several 3D tomogram measurements per second). Furthermore, HT provides quantitative imaging capability: RI maps of a cell are precisely and quantitatively measured, from which various cellular analysis can be followed. Employing HT, we address various biological and medical problems by phenotyping cell types from the measured 3-D RI tomograms of individual cells and training deep learning algorithms to rapidly and precisely classify cell types. We present applications in hematology, cell biology, and immunology. The potentials of the present approach for label-free imaging of individual bacteria and the species classification was discussed.

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Dr. YongKeun (Paul) Park is Associate Professor of Physics at KAIST. He earned a PhD in Medical Science and Medical Engineering from Harvard-MIT Health Science and Technology. Dr. Park's area of research is optics, holography, and biophysics. He has published over 110 peer-reviewed papers with over 5,300 citations, including 2 Nat Photon, 2 Nat Comm, 1 Science Advances, 4 PRL, 3 PNAS papers. He is a Fellow of Optical Society of American, and an Editor of Optics Express, Scientific Reports, Experimental



Biology and Medicine, and Current Optics and Photonics. Two start-up companies with close to 30 employees have been created from his research (Tomocube, The.Wave.Talk). To learn more about Prof. Park's research projects, visit his website: <u>http://bmol.kaist.ac.kr</u>. Work Interests: 1) Wave Physics; 2) Holography; 3) Biotechnology

# Session 4-2: Diagnostic Stewardship: the way forward to combating antimicrobial resistance

Margaret Ip, The Chinese University of Hong Kong, Hong Kong

Antimicrobial resistance (AMR) is an alarming concern. An estimated 700,000 people die of antimicrobial infections each year, and it was estimated that by 2050, 10 million lives a year and a cumulative 100 trillion USD of economic output are at risk. Much of the burdens of infections are projected in the South East Asia and the Western Pacific regions including China. Already, dwindling options of effective antibiotics are already compromising our treatment of common infections. Hong Kong is a cosmopolitan hub in a unique location within Asia that attracts an estimated 60M travellers annually, equating to approximately eight times its population. Besides, a large numbers of commuters cross the Hong Kong / Mainland border daily, serving a centre point to study AMR. Multidrug-resistant resistant organisms (MDROs) are not confined to healthcare settings, but carried in healthy individuals and found in our environment. With advancing technologies, new diagnostics may facilitate us for more judicious of antibiotics in both the community and healthcare settings. In this presentation some of these applications were discussed.

Dr. Margaret Ip is a Professor at the Department of Microbiology, Chinese University of Hong Kong and Honorary Consultant at the Prince of Wales Hospital, Shatin. She received her medical training at the University of Southampton and London School of Hygiene and Tropical Medicine, United Kingdom. She is a clinical microbiologist with over 20 years of experience in research on the epidemiology and antimicrobial resistance of clinically important bacterial pathogens, especially on Streptococcus pneumoniae and MRSA. She has a strong interest in the development and assessment of clinical diagnostic methods and new treatment modalities. She has published over 200 peer-reviewed papers. She serves as Advisor and Member in a number of Scientific Committees on antimicrobial resistance and



infection control and Associate Editors to Frontiers Microbiology and BMC Infectious Diseases, among others.

#### Session 4-3: Global genome epidemiology database (gGENEPID)

Makoto Kuroda, National Institute of Infectious Diseases, Japan

Next-generation sequencing (NGS) technology provides a comprehensive outline of pathogens based on its genome sequence. Currently, abundant genome sequences are available from public data source. Although this sounds to be a good situation for infection control on global and local outbreaks, the presence of a large excess of genome sequences may cause a confusion on how to utilise them properly, and to determine real epidemiological links based on the molecular markers.

Thus far, we have developed and released NGS web tools for pathogen genomics; MePIC2 for the detection of potential pathogens (PMID: 24451106); VirusTAP for *de novo* assembly of mammalian virus genome (PMID: 26870004); TGS-TB for *Mycobacterium tuberculosis* outbreak and antimicrobial resistance (AMR) (PMID: 26565975); AMiGA, for bacterial genome annotation. Here, we have constructed a global pathogen genome database gGENEPID (<u>https://gph.niid.go.jp/ggenepid/</u>) for further assistance in the prompt retrieval of essential genotypes of each publicly available bacteria pathogen genomes.

One of useful bacteria genome databases is, for instance, EnteroBase in UK (<u>https://enterobase.warwick.ac.uk/</u>) which supports the curation of multi-locus sequence typing (MLST) for *Enterobacteriaceae* including *E. coli, Salmonella* and *Vibrio*, and now expands genome epidemiology using core-genome SNPs phylogeny. Instead of EnteroBase and other databases, gGENEPID provides concise *in silico* predictions of MLST, AMR and pathogenicity for 35 bacteria pathogens listed in the Japanese Infectious Diseases Control Law (*Bacillus anthracis, Staphylococcus aureus, E. coli, Salmonella, Vibrio cholerae, M. tuberculosis*, NTM, *Bordetella pertussis*, etc).

Pathogen genomics is one of affordable approaches to determine all essence for genotype, AMR, and pathogenicity, and it is expected that big data could facilitate the outbreak control and a tailor-made medicine based on pathogen genomics.

Dr. Makoto Kuroda is the Director of the Pathogen Genomics Center at the National Institute of Infectious Diseases. He has as Assistant Professorship from the University of Tsukuba, and postdoctoral experience from the University of Washington.



### **Round Table Discussions**

#### One health in Asia

<u>Panellists:</u> Dr. Alicia Fajardo Lubian (Australia), Dr. Hoa Thi Ngo (Vietnam), Dr. Isabel Frost (CDDEP, India), Dr. Jie-Ming Qu (China), Dr. Seok Hoon Jeong (Republic of Korea) and Dr. Yohei Doi (Japan)

Dr Alicia Fajardo Lubian represented a team of National Health and Medical Research Council (NHMRC)-funded researchers at the University of Sydney and the Australian Gram-negative bacteraemia surveillance outcomes program. She introduced the session by giving an overview of the program. The panellists discussed challenges and opportunities for collaboration within their countries and with other Asian countries. A strong focus in the discussion was the connection between public health and animal health, with an identified gap in environmental surveillance of AMR. Discussions revealed that most countries have AMR policies and national plans but implementation of the policies and plans are a challenge.

#### Research collaboration in Asia

<u>Panellists:</u> Dr. Cai-Guang Yang (China, Academia, Novel Therapies), Dr. Kunihiko Nishino (Japan, Academia, Novel Therapies), Dr. Margaret Ip (Hong-Kong, Academia, Diagnostics), Dr. YongKeun Park (Korea, Academia, Diagnostics), Dr. Young Lag Cho (Republic of Korea, Industry, Novel Therapies)

The panellists recognised that scientific collaboration in Asia should be encouraged in order to become a key component of the global research efforts to tackle AMR. More dedicated funding and support to international collaborative efforts are needed to achieve that goal, but panellists were generally pleased with the support from their institutions and agreed that AMR is recognised as a key research area in Asia. Opportunities for research collaboration exist at regional and national levels but can be sometimes be difficult to identify, and the eligibility criteria and implementation of result-oriented consortia can become challenging even within one country. Dr. Aixin Yan from the University of Hong Kong and Dr. Kunihiko Nishino from Osaka University, Japan provided an overview of their collaboration, and YongKeun (Paul) Park from Korea provided an example of a successful tech transfer from academia to start up creation. The panellists raised the idea of writing a review article on the topic to raise awareness on the difficulties described.

### Annex 1. Workshop Program

Medical Building 3<sup>rd</sup> floor, Rm #713304 (Multimedia Room), Sungkyunkwan University School of Medicine.

Time	Speaker	Title	
09:00-10:30	Registration		
10:30-10:40	Dr. Seon-Won Kim National Research Foundation, Korea	Welcome address	
10:40-11:40	Keynote 1 & 2 Chair: Dr. Kyeong Kyu Kim (Sungkyunkwan University School of Medicine)		
10:40-11:10	Dr. Socorro Escalante World Health Organization	Medicines policies and health systems	
11:10-11:40	Dr. Laura Plant JPIAMR	JPIAMR: Global coordination of AMR research funding and activities	
11:40-11:45	Group Photograph		
11:45-13: 00	Lunch		
13:00-14:40	Session 1, Clinical Epidemiology of AMR in Asia, Chair: Dr. Jae-Seok Kim (Department of Laboratory Medicine, Kangdong Sacred Heart Hospital)		
13:00-13:25	Dr. Jie-Ming Qu Rui Jin Hospital, Shanghai Jiaotong University School of Medicine, China	Clinical and molecular characteristics of rapid- spreading carbapenem-resistant <i>Enterobacteriaceae</i> in China	
13:25-13:50	Dr. Yohei Doi Fujita Health University School of Medicine, Japan	Antimicrobial resistance (AMR) in Japan	
13:50-14:15	Dr. Seok Hoon Jeong Department of Laboratory Medicine, Yonsei University Severance Hospital, Korea	Current status of AMR in humans in South Korea: a report from Kor-GLASS	
14:15-14:40	Dr. Hoa Thi Ngo Zoonoses Group Oxford University Clinical Research Unit Vietnam	National action plans to combat antimicrobial resistance (AMR) in Vietnam and the high prevalence of AMR bacteria in community	
14:45-15:00	Break		
15:00-16:40	Session 2, AMR Policy and Funding in Asian Countries, Chair: Akhilesh K. Chaurasia (Sungkyunkwan University School of Medicine)		
15:00-15:25	Dr. Isabel Frost	Antimicrobial resistance (AMR) policy update in Asia	

#### Day 1: December 4, 2019

Time	Speaker	Title
	The Center for Disease Dynamics, Economics & Policy (CDDEP), India	
15:25-15:50	Dr. Yuxing Ni Dept. of Clinical Microbiology and Infection Control, Rui Jin Hospital, China	Containing AMR, China's action
15:50-16:15	Dr Shoji Miyagawa The Japan Agency for Medical Research and Development, Japan	AMR Action plan and funding in Japan
16:15-16:40	Dr. Kwang-Jun Lee Centres for Disease Control and Prevention, Korea	National strategies for the reduction of antimicrobial resistance: One Health
16:40-17:00	Break	
17:00-18:00	Round Table Discussion 1, One Health in Asia, Chair: Laura Plant (JPIAMR) Representative speakers in CDDEP, China, India, Japan, Republic of Korea and Vietnam	

#### Day 2: December 5, 2019

Time	Speaker	Title	
08:30-09:00	Registration		
09:00-10:00	Keynote 3 &4 Chair: Dr. Sang Hee Lee (Myongji University)		
09:00-09:30	Dr. Marc Lemonnier Antabio, France	Novel antibacterials targeting WHO's critical priority pathogens: challenges and opportunities from discovery to commercialization	
09:30-10:00	Dr. Choong-Min Ryu Korean Research Institute for Bioscience and Biotechnology, Republic of Korea	Diagnosis and combi-therapy against super-bacteria	
10:00-10:20	Break		
10:20-12:25	Session 3, Novel approaches for AMR Infections, Chair: Dr. Jae Hoon Yu (Seoul National University)		
10:20-10:45	Dr. Aixin Yan University of Hong Kong, Hong Kong	Native CRISPR-Cas mediated genome editing facilitates the treatment of clinical multidrug resistant <i>Pseudomonas aeruginosa</i> based on collateral sensitivity	
10:45-11:10	Dr. Young Lag Cho LegoChem Biosciences, Republic of Korea	Antibiotics pipeline for infectious diseases and development strategy of LegoChem Biosciences Inc.	

Time	Speaker	Title	
11:10-11:35	Dr. Kunihiko Nishino Osaka University, Japan	Multidrug efflux pumps in Gram-negative bacteria	
11:35-12:00	Dr. Cai-Guang Yang Shanghai Institute of Materia Medica, China	From antibiotic to antivirulence for AMR infection	
12:00-12:25	Dr. Xin-Shan Ye Peking University, China	Chemical modifications of aminoglycoside antibiotics and beyond	
12:25-13:30	Lunch		
13:30-14:45	Session 4, New technologies in AMR diagnostics Chair: Dr. Kin-Ming (Clement) Tsui (Weill Cornell Medicine - Qatar; Sidra Medicine)		
13:30-13:55	Dr. YongKeun Park KAIST and Tomocube Inc, Republic of Korea	Holotomography and artificial intelligence: label- free 3D imaging and analysis of individual live cells	
13:55-14:20	Dr. Margaret Ip The Chinese University of Hong Kong, Hong Kong	Diagnostic Stewardship: The way forward to combating antimicrobial resistance	
14:20-14:45	Dr. Makoto Kuroda National Institute of Infectious Diseases, Japan	Global genome epidemiology database (gGENEPID)	
14:45-15:00	Break		
15:00-16:00	Round Table Discussion 2, Research collaboration in Asia Chair: Marc Lemonnier (Antabio) Representative speakers in China, Hong Kong, Japan, and Republic of Korea with industrial and academic backgrounds		
16:00-16:20	Dr. Laura Plant JPIAMR	Closing remarks	

Name	Affiliation	Country
Ahad, Abdul	National Institute of Health Islamabad	Pakistan
Ali, Zulfiqar	PCSIR Laboratories Complex Karachi	Pakistan
Arya, Rekha	Sungkyunkwan University	Republic of Korea
Bae, Hee-Won	CHA University	Republic of Korea
Batool, Nayab	Sungkyunkwan University	Republic of Korea
Chaurasia, Akhilesh K.	Sungkyunkwan University	Republic of Korea
Cho, You-Hee	CHA University	Republic of Korea
Cho, Young Lag	LegoChem Biosciences	Republic of Korea
Choi, Hyun Kyung	Jungwon University	Republic of Korea
Chung, Sung Hee	Hallym University	Republic of Korea
Doi, Yohei	Fujita Health University School of Medicine	Japan
Escalante, Socorro	World Health Organization	Vietnam
Fajardo-Lubián, Alicia	The University of Sydney	Australia
Frost, Isabel	The Center for Disease Dynamics, Economics & Policy	India
Fujii, Daisuke	Cabinet Secretariat	Japan
Homma, Misa	Japan Agency for Medical Research and Development	Japan
Ip, Margaret	The Chinese University of Hong Kong	Hong Kong
Jeon, Jeong Ho	Myongji University	Republic of Korea
Jeong, Seok Hoon	Yonsei University	Republic of Korea
Jo, Hyejun	Jeju National University	Republic of Korea
Kang, Lin-Woo	Konkuk University	Republic of Korea
Kim, Bi-o	CHA University	Republic of Korea
Kim, Inhee	Hallym University	Republic of Korea
Kim, Jae-Seok	Kangdong Sacred Heart Hospital	Republic of Korea
Kim, Jung-Min	Hallym University	Republic of Korea
Kim, Hun	Sungkyunkwan University	Republic of Korea
Kim, Kyeong Kyu	Sungkyunkwan University	Republic of Korea
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Lade, Harshad	Kangdong Sacred Heart Hospital	Republic of Korea
Lee, Jung Hun	Myongji University	Republic of Korea

# Annex 2. Speakers and Participants

Lee, Kwang Jun	Centre for Disease Control and Prevention	Republic of Korea
Lee, Sang Hee	Myongii University	Republic of Korea
Lee, Won Sik	Sungkyunkwan University	Republic of Korea
Lemonnier, Marc	Antabio	France
Miyagawa, Shoji	The Japan Agency for Medical Research and Development	Japan
Ngo, Thi Hoa	Oxford University	Vietnam
Nguyen, An	Pham Ngoc Thach University of Medicine	Vietnam
Nguyen, Trung Thanh	Centre for Tropical Medicine Oxford University	Vietnam
Ni, Yuxing	Rui Jin Hospital	China
Nishino, Kunihiko	Osaka University	Japan
Noda, Hiroyuki	Coordination office of Measures on Emerging Infectious Disease	Japan
Oh, Changsuk	Sungkyunkwan University	Republic of Korea
Park, YongKeun	KAIST and Tomocube Inc	Republic of Korea
Park, Hyung Soon	NosQuest/ASTA	Republic of Korea
Plant, Laura	Joint Programming Initiative on Antimicrobial Resistance	Sweden
Qu, Jie Ming	Rui Jin Hospital	China
Ryu, Choong-Min	Korean Research Institute for Bioscience and Biotechnology	Republic of Korea
Raza, Shahbhaz	Jeju National University	Republic of Korea
Sajjad, Wasim	National University of Medical Sciences	Pakistan
Sultan, Maria	Sungkyunkwan University	Republic of Korea
Tang, Arthur	Sungkyunkwan University	Republic of Korea
Thu, Tran Thi Anh	Oxford Clinical research Unit	Vietnam
Trung, Nguyen	Oxford University	Vietnam
Tsui, Kin Ming	Sidra Medicine/Weill Cornell Medicine - Qatar	Qatar
Xu, Yanping	Ruijin Hospital	China
Yan, Aixin	The University of Hong Kong	Hong Kong
Yang, Cai-Guang	Shanghai Institute of Materia Medica	China
Ye, Xin-Shan	Peking University	China
Yu, Jae Hoon	Seoul National University	Republic of Korea
Zhang, Yibo	Rujin Hospital	China